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10/506,805

01/19/2005

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EXAMINER

PURDY, KYLE A

ART UNIT

PAPER NUMBER

1611

MAIL DATE

DELIVERY MODE

03/06/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|-------------------------------------|--|
| Office Action Summary | Application No. 10/506,805 | Applicant(s) LEWIS ET AL. | |
| | Examiner Kyle Purdy | Art Unit 1611 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09/07/2004, 01/19/2005 and 01/11/2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16, 20-35, 37, 38 and 42-56 is/are pending in the application.
- 4a) Of the above claim(s) 29-35 and 45-56 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16, 20-28, 37, 38 and 42-44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1 sheet (01/11/2008)</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election Acknowledged

1. Applicants' election with traverse the invention of Group I encompassing claims 1-16, 20-28, 37,38 and 42-44 is acknowledged. The traversal is on the grounds that the teaching of Konno et al. does not teach the special technical feature present in Groups I and II. Specifically, the special technical feature is that the copolymer contains a hydrophobic block and a hydrophilic block, dispersed in solution, and a biologically active compound associated with the polymer, wherein the hydrophilic block has pendant zwitterionic groups. Applicants arguments are persuasive.

2. A new reference is being applied in order to break unity between Groups I and II. The common feature of a copolymer having a hydrophobic block and a hydrophilic block, dispersed in solution, and a biologically active compound associated with the polymer, wherein the hydrophilic block has pendant zwitterionic groups can not qualify as a special technical feature as it does not provide a contribution over the prior art because it is disclosed by the teaching of Lobb et al. (J. Am. Chem. Soc., 2001, 123(32), 7913-7914). Lobb et al. teaches a copolymer having a hydrophobic block and a hydrophilic block, dispersed in solution, and a biologically active molecule associated with the polymer, wherein the hydrophilic block has pendant zwitterionic groups (see 102(a) discussion below). Therefore, Groups I and II lack unity as the reference specifically suggests the claimed elements.

3. Claims 1-16, 20-35, 37, 38 and 42-56 are pending and claims 17-19 and 39-41 are canceled. Claims 1-16, 20-28, 37-38 and 42-44 are presented for examination on the merits. The following rejections are made.

Response to Amendments/Arguments

4. The declaration under 37 CFR 1.132 filed on January 7, 2008 is sufficient to overcome the lack of unity between Groups I and II and rejections of claims 1- 28 and 37-44 based upon USC 35 102(a) and 35 USC 103(a).

Information Disclosure Statement

5. The reference of Konno et al. to “Enhanced solubility of paclitaxel using water-soluble.....polymers” included in the IDS submitted January 11, 2008 was not considered because the publication fails to list the date of publication.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

7. Claims 1, 4-14, 20-25, 38 and 42-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Lobb et al. (J. Am. Chem. Soc., 2001, 123, 7913-7914; of record).

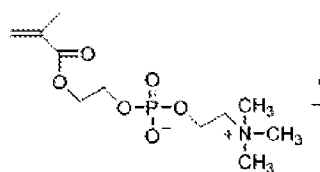
8. Lobb et al. (‘Lobb) discloses the synthesis of a biocompatible phosphorylcholine-based methacrylate copolymer. The copolymer is an amphiphilic block copolymer having a hydrophilic block and in the solution, and a biologically active compound associated with the polymer [fibrinogen] (see page 7914, left column 2nd paragraph; see instant claim 1), wherein the

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hydrophilic block has pendant zwitterionic groups (see Figure 2; structure; see instant claim 1).

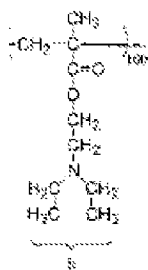
The copolymer is in the form of micelles (see Figure 2, 'DEA core micelles'; see instant claim

4). The hydrophilic block is formed by radical polymerization of the ethylenically unsaturated monomers (see page 7913, left column, 2nd paragraph; see instant claim 5). The hydrophilic monomers comprise a zwitterionic monomer having the following structure:



(see Figures 1 and 2; see instant claim 6-12 and 38).

9. The hydrophobic block comprises a pendant group which is ionizable and possesses a pKa or pKb in the range of 4 to 10 (see Figure 2, structure). The hydrophobic structure is shown below:



10. The pKa for the hydrophobic structure is 9.17 (see STN search of structure b; see instant claim 13). The hydrophobic block is polymerized by radical polymerization of the ethylenically unsaturated monomers (see page 7914, left column, 4th paragraph; see instant claim 14). The degree of polymerization for the hydrophilic block is 30 (see Figure 2, structure; see instant claims 21 and 43) and the degree of polymerization for the hydrophobic block is 100 (see Figure 2, structure; see instant claims 22 and 44). The ratio for the degrees of polymerization is 10:3

which falls within the range of 1:5 to 10:1 (see Figure 2, structure; see instant claim 23). The polymerization process for polymerizing the hydrophilic block is via atom transfer radical polymerization (see page 7913, left column, 2nd paragraph; see instant claims 24-25).

11. Thus, the limitations of the instant claims are met entirely by the reference of Lobb.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. Claims 2, 3, 28 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lobb et al. (J. Am. Chem. Soc., 2001, 123, 7913-7914; of record) in view of Konno et al. (Biomaterials, 2001, 22, 1883-1889; of record).

14. Lobb is relied upon for disclosure described in the rejection of claim 1 under 35 U.S.C.102(a).

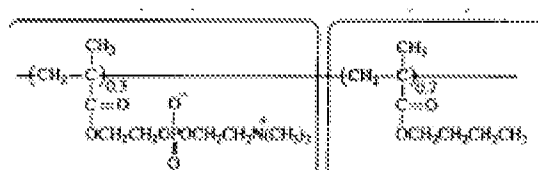
15. Lobb fails to teach the biologically active molecule as being a cytotoxic molecule which is associated with the copolymer through hydrophobic interactions wherein the biologically active molecule has a partition coefficient between octanol and water of at least 1.5.

16. Konno et al. ('Konno) is drawn to the preparation of nanoparticles composed with bioinspired 2-methacryloyloxyethyl phosphorylcholine polymer (see Figure 1, MPC unit). The synthesized particles possess hydrophilic and hydrophobic monomers. A specific example of the

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hydrophilic/hydrophobic monomers copolymerized and MPC and butyl methacrylate (BMA).

The structure is shown below:



(see Figure 1).

These amphiphilic copolymers are useful because they provide a convenient means for delivering drugs or fluorescent molecules to the body without eliciting an immune response (see page 1883, left column, 1st paragraph). That is, the particles possess good biocompatibility, much like that of Lobb. The particles may be used to carry and delivery fluorescent molecules for imaging and for carrying drugs. It is taught that the absorption of drugs and other molecules to the copolymer occurs through hydrophobic interaction (see page 1884, left column, 1st paragraph). An exemplified species taught to be absorbed to the copolymer is that of N-phenyl-1-naphthylamine (NPN) and bovine serum albumin (see page 1885, Experimental: 2.4 and 2.5). NPN possess an octanol:water partition coefficient of at least 1.5 (see physical properties section of IPCS INCHEM reference). Additionally, according to the INCHEM reference, NPN is extremely toxic to aquatic organisms.

17. Thus it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Lobb and Konno with a reasonable expectation for success in arriving at a composition comprising an amphiphilic block copolymer having a hydrophilic and a hydrophobic block, dispersed in solution, and a biologically active compound associated with the polymer which has a partition coefficient of at least 1.5 and is associated with the hydrophobic portion of the polymer, wherein the hydrophilic block as pendant zwitterionic

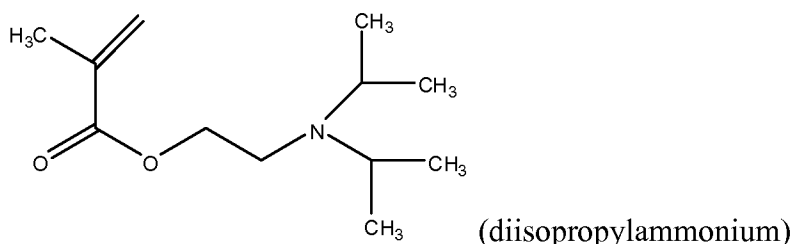
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groups. The significance of Lobb is that the reference teaches the procedure for synthesizing a block copolymer via atom transfer radical polymerization wherein the copolymer contains a hydrophobic and a hydrophilic block, the hydrophilic block possessing a zwitterionic group. Moreover, Lobb teaches that the synthesized copolymers can be used to produce biocompatible surfaces and shows considerable promise for drug delivery applications. However, Lobb fails to teach the biologically active compound as being associated with the hydrophobic portion of the copolymer and having a partition coefficient of at least 1.5. The teaching of Konno cures these deficiencies. Konno teaches using a copolymer for delivering biologically active agents. One such agent being NPN which is associated with the hydrophobic portion of the copolymer due to its hydrophobic nature. Albeit the reference of Konno is drawn to a random copolymer, it appears that the copolymers properties are essentially the same to the copolymer of Lobb. Moreover, if NPN were employed in the reference of Lobb, one would reasonably expect the molecule to interact with the hydrophobic portion of the block copolymer as it did in the reference of Konno. Therefore, the invention as a whole is *prima facie* obvious to one ordinarily skilled in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

18. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lobb et al. (J. Am. Chem. Soc., 2001, 123, 7913-7914; of record).

19. Lobb is relied upon for disclosure described in the rejection of claims 1, 13 and 14 under 35 U.S.C.102(a).

20. Lobb fails to disclose the hydrophobic block as possessing the following monomeric structure



21. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teaching of Lobb to arrive at diisopropylammonium but substituting a hydrogen with a methyl in the diethylammonium present in the teaching of Lobb. The major difference between the teaching of Lobb and the instant claims is that the monomer of the instant claims has a methyl rather than a hydrogen. The presence of a methyl group in place of a hydrogen does not give patentable momentum to the recited species. It is well established that a methyl functionality is structurally analogous to a hydrogen, and absent any secondary result, the elected species would possess the same functional properties as that of diethylammonium. Therefore, the invention as a whole is *prima facie* obvious to one ordinarily skilled in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

22. Claims 20 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lobb et al. (J. Am. Chem. Soc., 2001, 123, 7913-7914; of record) in view of Coessens et al. (Prog. Polym. Sci., 2001, 26, 337-377; of record).

23. Lobb is relied upon for disclosure described in the rejection of claim 1 under 35 U.S.C.102(a).

24. Lobb teaches that the polydispersity of the MPC homopolymer block is from between 1.23 to 1.45 (see page 7914, left column, 2nd paragraph).

25. Lobb specifically fails to teach the polydispersity for the hydrophobic block of the copolymer.

26. However, Coessens which is drawn to describing in detail the properties generally associated with atom transfer radical polymerization process, teaches that atom transfer radical polymerization creates well-defined, precisely controlled polymers with polydispersities generally lower than 1.3 (see Coessens, page 339, last paragraph).

27. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Lobb and Coessens with a reasonable expectation for success in arriving at a composition comprising an amphiphilic block copolymer having a hydrophilic and a hydrophobic block, dispersed in solution, and a biologically active compound associated with the polymer, wherein the hydrophilic block as pendant zwitterionic groups wherein the polydispersity of molecular weight of each block is from 1.1 to 1.4. Although Lobb is silent to the polydispersity of the hydrophobic block, the block if synthesized by atom transfer radical polymerization would most likely have a polydispersity of below 1.3. Therefore, the invention as a whole is *prima facie* obvious to one ordinarily skilled in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

28. Claims 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lobb et al. (J. Am. Chem. Soc., 2001, 123, 7913-7914; of record).

29. Lobb is relied upon for disclosure described in the rejection of claims 1, 24 and 25 under 35 U.S.C.102(a).

30. Lobb teaches that the atom transfer radical polymerization initiator is that of oligo(ethylene glycol) bromide (OEGBr). OEGBr is a hydrophobic polymer compound and is taught to be used for the synthesis of the MPC homopolymer (see page 7913, right column, 2nd paragraph). It is also taught that that MPC diblock copolymers can also be synthesized via atom transfer radical polymerization (see page 7914, left column, 4th paragraph).

31. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use and modify the teaching of Lobb with a reasonable expectation for success in arriving at a composition comprising an amphiphilic block copolymer having a hydrophilic and a hydrophobic block, dispersed in solution, and a biologically active compound associated with the polymer, wherein the hydrophilic block as pendant zwitterionic groups wherein the hydrophobic block is synthesized via a initiator possessing a hydrophobic polymeric moiety. Although Lobb does not specifically teach OEGBr as being used in the synthesis of the hydrophobic block, its use in such a process would be motivated by Lobbs teaching. If such an undertaking lead to the success of the invention, then it is likely not the product of innovation, but rather a product of common sense and ordinary skill. Additionally, the hydrophobic block taught by Lobb is formed via synthesis of the ethylenically unsaturated moieties by radical transfer polymerization. Therefore, the invention as a whole is *prima facie* obvious to one ordinarily skilled in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

32. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kyle A. Purdy whose telephone number is 571-270-3504. The examiner can normally be reached from 9AM to 5PM.

33. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

34. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*/Kyle Purdy/
Examiner, Art Unit 1611
February 26, 2008*

*/Michael P Woodward/
Supervisory Patent Examiner, Art
Unit 1615*